UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/227,518	01/08/1999	BERNARD ROBERT TERRY	5441.200-US	8122

2292 7590 11/05/2002

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
GABEL, GAILENE

ART UNIT	PAPER NUMBER
1641	20

DATE MAILED: 11/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/227,518	Applicant(s) TERRY ET AL.	
	Examiner Gailene R. Gabel	Art Unit 1641	

-- The MAILING DATE f this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2002 and 23 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/2/02 has been entered.

Amendment Entry

2. Applicant's amendment and response filed 1/23/02 in Paper No. 14 is acknowledged and has been entered. Claims 18-38 have been cancelled. Claims 39-59 have been added. Further, Applicant's amendment and response filed 7/2/02 in Paper No. 19 is also acknowledged and has been entered. Claims 39-58 have been amended. Currently, claims 39-59 are pending and are under examination.

Rejections Moot or Withdrawn

3. The rejection of claims 18-38 under 35 U.S.C. 112, 102, and 103 are now moot in light of Applicant cancellation of the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 39-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39, at steps b) and c), is ambiguous in reciting, "bringing the array of test compounds in close apposition with a detector layer" and "detecting a response" because it is unclear how a response can be elicited by the detector layer, i.e. viable cells, in the absence of actual direct contact and application of the test compounds upon the cellular detector layer, or an element, i.e. liquid, that allows contact and diffusion of the test compound into the cellular detector layer.

Claim 39, at steps c) and d), is vague and indefinite because it is unclear how an identity of each of the test compounds is indicated and determined only by a 2-dimensional coordinate. It appears that as recited, at most, only the position of the test compound can be identified. See page 8, line 9 of the specification.

Alternatively, claim 39 is indefinite as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. Specifically, it appears that to allow the identity of the test compounds to be identified, the response elicited by the test compound in question should be correlated and compared to a chosen known standard. See page 17, last full paragraph and page 31, first full paragraph, specifically, lines 17-24.

Claim 58 at steps a) and b), is ambiguous in reciting, "bringing the array of test compounds in close apposition with a detector layer" and "detecting a response"

because it is unclear how a response can be elicited by the detector layer, i.e. viable cells, in the absence of actual direct contact and application of the test compounds upon the cellular detector layer, or an element, i.e. liquid, that allows contact and diffusion of the test compound into the cellular detector layer.

Claim 58 at step c) is vague and indefinite because it is unclear how an identity of each of the test compounds is indicated and determined only by a 2-dimensional coordinate. It appears that as recited, at most, only the position of the test compound can be identified. See page 8, line 9 of the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The claims are understood to be drawn to a screening method of test compounds which are disposed on a solid support in a pattern, i.e. grid with rows and columns, which can be identified by a 2-dimensional coordinate. 2-dimensional coordinate is defined and identified by a position that intersects a given X and Y axis. Accordingly,

5. Claims 39, 41-45, 51, 53-54, 56, 58-59 are rejected under 35 U.S.C. 102(e) as being inherently anticipated by Negulescu et al. (US 6,214,563).

Negulescu et al. disclose cell-based assays for use in drug discovery to screen large numbers of test compounds for bioactivity. Specifically, Negulescu et al. disclose providing an array of test compounds, stored in addressable chemical wells, i.e. in a pattern or grid (thus, identifiable by 2 dimensional coordinate), having a programmable selection and retrieval system which brings the test compounds into contact with a cellular detector layer (see column 17, lines 7-12). Negulescu et al. disclose that the cellular detector layer (membrane compartment) comprises physiologically viable cells that are disposed on addressable wells of a microtiter plate. The cellular detector layer is physically and optically disposed upon optical sensing surface of the microtiter wells, so as to allow transmission, i.e. optically clear, and passage of light at a wavelength for detection (see column 3, lines 10-16 and column 13, lines 46-55). The viable cells on the detector layer preferably form a monolayer (single layer) (see column 14, lines 5-10). After contact between the test compound and the cellular detector layer, bioactivity is detected using different fluorescent monitoring systems including those adapted for high throughput screening using multi-well platforms (see column 16, line 63 to column 17, line 3 and lines 44-47). If the test compound has bioactivity as a candidate modulator, there is a change in the fluorescence or luminescence property of the cellular detector layer disposed on microtiter wells, and the change is determined by an illumination system by exciting the fluorescent reporter on the detector layer with various selected wavelengths (see columns 22 and 23).

6. Claims 39-42, 45, 48-49, 51-55, and 58-59 are rejected under 35 U.S.C. 102(e) as being inherently anticipated by Chelsky et al. (US 5,856,083).

Chelsky et al. disclose a lawn assay for screening and determining test compounds that are held on porous or non-porous solid support (see column 3, lines 30-67, column 5, lines 15-52, and column 6, lines 62-67). Chelsky et al. disclose providing test compounds linked to the support by a cleavable linker and upon cleavage of the linker, the test compounds diffuse into a support's vicinity comprising a colloidal matrix or a scintillant coated surface so that high concentrations of the test compounds are created on these supports (see column 3). Test compounds released are then contacted with a detector layer comprising cellular receptors, i.e. membrane bound receptors, disposed on the scintillant supports so that binding interaction therebetween can be detected and measured using a fluorescence detection and illumination systems (see column 4, specifically lines 51-61). Chelsky et al. also specifically disclose providing the test compounds as preferably arranged in ordered array, i.e. in a pattern or grid, (thus, identifiable by 2 dimensional coordinate) to allow easier identification of those that have bioactivity. Specifically, the array can be ordered so that the position of the test compound corresponds to the identity of the compound (see column 7). Chelsky et al. teach application of the invention in combinatorial libraries and drug discovery assays.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 46-47, 50, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chelsky et al. (US 5,856,083) in view of Sittampalam et al. (Current Opinion in Chemical Biology, 1997).

Chelsky et al. has been discussed supra. Chelsky et al. differ from the instant invention in failing to disclose that the detector layer is a pH sensing surface and a temperature sensing surface. Chelsky et al. also differ from the instant invention in failing to disclose growing cells on a porous membrane of a solid support.

Sittampalam et al. teach cell based assay systems for use in high throughput screens wherein physiologically viable cells are coated and grown onto a detector layer made from scintillant plastic so that upon contact with a test compound, the cells are

monitored for bioactivity (cellular events, cytosolic calcium mobilization) (see page 365, column 1). The scintillant plastic is incorporated on 96 microwell plates wherein its surface is able to function as a pH sensing surface or a temperature sensing surface (see page 386, column 2). Sittampalam et al. also teach that illumination systems such as FRET systems are capable of exciting fluorescence of the detector layer and detecting changes in fluorescence or luminescence properties of the cells (see page 388, column 1). Sittampalam et al. teach that the most common method for detecting ligand interaction between test compounds (drugs) and targets in cells is to employ reporter genes.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to grow physiologically viable cells as taught by Sittampalam on the solid matrix in the method of Chelsky because use of fresh growing cells provides for ensuring increased viability of cells in detecting bioactivity of test compounds. Additionally, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the pH sensing surface and temperature sensing surface taught by Sittampalam into the scintillant support taught by Chelsky upon which the cellular detector layer is disposed because Sittampalam specifically taught that such features allow accurate measurements of cellular biochemistry in confluent layers of cells at the bottom of the plates or support.

Response to Arguments

8. Applicant's arguments filed 8/6/01 have been fully considered but they are not persuasive.

A) Applicant argues that Negulescu et al. does not describe a key feature of the present invention, namely, an array of test compounds disposed on a solid support wherein the position of each compound on the solid support is denoted by a simple 2-dimensional coordinate.

In response, Negulescu et al. at column 17, lines 7-13 discloses that the array of test compounds are provided as arranged in a pattern of addressable chemical wells in multiwell platforms; thus, the chemical wells are at positions inherently identifiable and denoted by a 2 dimensional coordinate.

B) Applicant argues that Chelsky et al. disclose merely an arrangement, but not an array, that can be identified by a simple 2-dimensional arrangement. Applicant further contends that detection of bioactivity in the method of Chelsky et al. requires decoding.

Contrary to Applicant's argument, Chelsky et al. at column 7, lines 36-43, taught that the arrays are preferably ordered so as to provide advantage (usefulness) in identifying the compound by virtue of the *zone* of activity and *position* corresponding to the identity of the compound. A zone or position in a given pattern or grid are defined and identified by a position that intersects a given X and Y axis; thus identified by a 2-dimensional axis. Further contrary to Applicant's contention, a step of decoding is not a requirement in the method of Chelsky, but rather a preferred method for identifying the

test compounds. Such decoding step requires incorporation of chemical tags that encode the identity of test compounds.

9. No claims are allowed.

Remarks

10. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Schulleck et al. (Analytical Biochemistry, 1996) teach high density screening format for encoded combinatorial libraries wherein the libraries are bead-based and dispersed upon 2-dimensional gels of thin layer matrices or agarose.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800/1641

Gailene R. Gabel
October 30, 2002